Remarks

Claims 1, 39, 40, 60-85, and 87-97 are pending in the application following entry of this Amendment. Claims 58, 59, and 86 have been canceled. Claims 1 and 40 stand withdrawn from consideration. Claims 39, 61-65, 70, 73-75, 77, 84, 85, 87, and 92 have been amended. Claims 95-97 have been added. Claim 39 is the only independent claim pending and not withdrawn. No additional claim fee is believed due, because three claims have been canceled and three dependent claims have been added.

No new matter is added by the amendments and additions made herein. Support for the amendments is found in the specification as follows.

The amendment to specification paragraph **[0034]** merely corrects an obvious error relating to stray keystrokes.

The amendment to specification paragraph **[0037]** merely corrects an obvious error relating to a missing comma.

The text added to claim 39 has antecedent basis earlier in claim 39.

Claim 61 has been amended simply to clarify that "the genes" referred to therein are the "four genes" recited in claim 60, from which claim 61 depends.

The amendments made to claims 62-65 simply import language from claim 39, from which each of the amended claims directly or indirectly depends.

Item ix) in each of claims 62 and 87 has been amended to include both oxidoreductases that are disclosed in the specification at page 10, line 21, of the specification. A comma has been added at the end of item xv) in each of claims 62 and 87, which is simply an obvious grammatical correction.

The amendments made to each of claims 70, 73-75, and 77 simply clarify the wording that was already present therein.

The amendments made to claims 84, 85, and 87 simply conform the language of those claims to deletion from claim 39 of items d) and e) and to cancellation of claim 86.

The amendment made to claim 92 simply imports language from claim 39, from which the amended claim depends.

Each of the Examiner's objections or rejections is addressed below in the order they were presented in Paper No. 7.

Rejections Pursuant to 35 U.S.C. § 112, Second Paragraph

The Examiner rejects claims 39 and 58-94 pursuant to 35 U.S.C. § 112, second paragraph, for various reasons, as indicated in items 3A-3F on pages 2 and 3 of the Office Action. The Applicants respond to the items individually below.

In item 3A, the Examiner objects to language relating to "genes which encode a protein that indirectly affects oxidative stress." This text has been deleted from the claims, and this portion of the Examiner's rejection is moot.

In item 3B, the Examiner objects to language relating to "genes which encode a protein for which the level of expression of the protein is associated with oxidative stress." This text has been deleted from the claims, and this portion of the Examiner's rejection is moot.

In item 3C, the Examiner suggests that the terms "the composition" and "the polymorphisms" lack antecedent basis because the designations "**anti-oxidant**" composition and "**disorder-associated**" polymorphisms were not used. Although the Applicants believe that it is unnecessary to do so (i.e., the claims recite only a single type of composition and a single type of polymorphisms, which must therefore be the ones referred to), the Applicants have amended the claims to supply these designators at every instance where "composition" and "polymorphisms" occur in the claims. This portion of the Examiner's rejection is moot.

In item 3D, the Examiner objects to the phrase "assessing occurrence in the human's genome of disorder-associated polymorphisms." The Examiner suggests that the meaning of this phrase is unclear. The Applicants respectfully suggest that the meaning of the phrase is not unclear. The phrase simply refers to analyzing the genome of a human being and assessing whether certain disorder-associated polymorphisms (DAPs) occur in the human's genome. The process is briefly described in paragraph **[0015]** on page 6 of the specification and described in greater detail thereafter. "Disorder-associated" polymorphisms are defined in paragraph **[0019]** on page 7 of the specification and described in greater detail on pages 9-13 of the specification. If the Examiner believes that the phrase would be more easily understood if it were transposed to read "assessing occurrence of disorder-associated polymorphisms in the

human's genome," then the Applicants would be willing to amend the claim accordingly (i.e., this change does not alter the meaning of the claim).

In item 3E, the Examiner objects to the term "the genes" as used in claims 62-69. In the Examiner's view, it was not clear to which genes this term referred. The Applicants have amended claims 62 (from which claim 66-69 depend) and 63-65 in a manner that they believe clarifies which genes are being referred to. The Applicants respectfully contend that these amendments overcome the portion of the Examiner's rejection relating to claims 62-69.

In item 3F, the Examiner objects to the term "higher stringency" in claims 70-81. In the Examiner's view, the meaning of the term is unclear. The Applicants have amended claims 70, 73-75, and 77 to clarify that the characteristics of the "first oligonucleotide" (the "second oligonucleotide" in claim 77). To the extent that the Examiner's comments might reflect a belief that a skilled artisan would not understand what is claimed, the Applicants respectfully contend that a skilled artisan in this field knows many ways to detect a particular nucleotide sequence using standard methods based on nucleic acid hybridization. The skilled artisan would understand claims 70-81 to encompass use of any of those standard methods to determine the sequence of a human's genome at a polymorphic position. In view of the knowledge of skilled artisans in this field, the Applicants respectfully contend that none of claims 70-81 is unclear.

In view of the above comments, the Applicants request that the Examiner reconsider and withdraw the rejection of claims 39 and 58-94 pursuant to 35 U.S.C. § 112, second paragraph.

Rejection Pursuant to 35 U.S.C. § 112, First Paragraph (Written Description)

The Examiner rejects claims 39 and 58-94 pursuant to 35 U.S.C. § 112, first paragraph. In the Examiner's view, the specification does not adequately convey to a skilled artisan that the Applicants were in possession of the claimed invention at the time the application was filed. The Examiner included two apparently alternative grounds for this rejection, in the section numbered "1)" on page 5 of the Office Action and in the section numbered "2)" on page 6 thereof. The Applicants respond separately below to the two alternative grounds.

1) Genus/Species Encompassed by Each of Items a)-e) in Claim 39

The Examiner recognizes that each of items a)-e) of claim 39 recites a genus of genes. The Applicants note that items d) and e) have been deleted from claim 39, and that the Examiner's rejection is therefore moot as it relates to those two items. With regard to items a)-c) of claim 39, the Applicants disagree with the Examiner's contention that the particular genes disclosed in the specification are not representative of each genus in items a)-c).

The genus of genes recited in item a) of claim 39 encompasses all human genes that encode an enzyme that catalyzes conversion of a toxic oxygen species to a less toxic oxygen species. Specific examples of these genes that are disclosed in the specification and claimed include those which encode mitochondrial manganese superoxide dismutase (MnSOD), cytoplasmic copper/zinc superoxide dismutase (CZSOD), catalase, and glutathione peroxidase (GP). These genes are representative of human genes known to encode an enzyme that catalyzes conversion of a toxic oxygen species to a less toxic oxygen species.

The genus of genes recited in item b) of claim 39 encompasses all human genes that encode a protein that provides protection against oxidative stress (OS). Specific examples of these genes that are disclosed in the specification and claimed include those which encode MnSOD, CZSOD, catalase, GP, glutathione S-transferase, glutathione reductase, thioredoxin reductase, paraoxonase, NAD(P)H:quinone oxidoreductases 1 and 2, 8-oxo-7,8-dihydrodeoxy-guanosine triphosphatase, epoxide hydrolase, and heat shock proteins. These genes are representative of human genes known to encode a protein that provides protection against OS.

The genus of genes recited in item b) of claim 39 encompasses all human genes that encode a protein that induces production of a toxic oxygen species. Specific examples of these genes that are disclosed in the specification and claimed include those which encode include myeloperoxidase, NADH/NADPH oxidase p22 phox protein, nitric oxide synthase, xanthine oxidase, and cytochrome P450. These genes are representative of human genes known to encode a protein that induces production of a toxic oxygen species.

For each of items a), b), and c) of claim 39, the specification discloses genes that represent substantially all of the human genes of the corresponding genus. The Applicants respectfully contend that this disclosure must be a representative sample of the genes of each genus. The claims recite these genes as genera because if another gene (e.g., a second human

paraoxonase gene) were to be hereafter discovered, it would be immediately apparent to a skilled artisan that a DAP in the newly-discovered gene could be used in the same manner as DAPs of the known genes.

For the foregoing reasons, the Applicants respectfully contend that the specification provides sufficient representative examples for each genus of genes recited in items a)-c) of claim 39.

2) Disorder-Associated Polymorphisms Associated with Genes Recited in Items a)-e) in Claim 39

The Examiner identifies that the Applicants have disclosed many DAPs (i.e., 18 on pages 11-13 of the specification), but suggests that there is a "large" to "unlimited" number of possible polymorphisms that can be used to practice the claimed invention. The Examiner suggests that because the specification does not list every DAP that could conceivably be used in the claimed methods, the claims are not supported by a sufficient written description. The Applicants respectfully contend that the Examiner misunderstands the meaning of the term "disorder-associated polymorphism," what is taught in the specification, and what is claimed, as explained in the following paragraphs.

The Applicants have not simply discovered that several specific genetic polymorphisms are associated with the susceptibility of a human to OS. Instead, the Applicants have made the much broader discovery that a human's susceptibility to OS is affected by occurrence of a genetic polymorphism in any gene of several classes of genes, wherein occurrence of the polymorphism is correlated with a disorder (i.e., not necessarily a disorder related to OS). Put another way, a polymorphism in any of those relevant genes that is sufficiently detrimental to be manifested (even in only some humans) as a disorder is sufficient to increase the susceptibility of a human to OS. Thus, by analyzing occurrence in a human's genome of these detrimental polymorphisms, one can estimate the susceptibility of that human to oxidative damage and select an appropriate dose of an anti-oxidant composition to administer to the human.

The term "disorder-associated polymorphism" is defined in the specification in paragraph **[0019]** at page 7, lines 15-17. The definition indicates that every DAP has been

correlated with occurrence of a disease or pathological state in a human. Thus, the term includes only polymorphisms for which such a correlation is known - it does not include polymorphisms that are not known to be correlated with a disease or pathological state.

The 18 polymorphisms that the Applicants have identified at pages 12 and 13 of the specification are not simply any polymorphisms that occur in the corresponding genes, but are instead disorder-associated polymorphisms - the occurrence of each has been correlated with a disease or pathological state in humans. The Applicants' invention is not limited to these 18 DAPs, but instead can be practiced using any polymorphism in a gene recited in the claims that is hereafter linked with occurrence of a disease or pathological state in a human. This is because as soon as the DAP is identified, its usefulness in the claimed methods will be immediately apparent to a skilled artisan. Because "disorder-associated polymorphism" has been defined as it has in the specification, assessing occurrence of a polymorphism in a claimed gene would not be within the scope of the claims unless and until occurrence of the polymorphism were identified as a DAP. Thus, the Applicants are claiming no more than the subject matter that they have invented.

For the foregoing reasons, the Applicants respectfully contend that they are entitled to recite "disorder-associated polymorphisms," as this term is defined in the specification, in the claims.

The Examiner is respectfully requested to reconsider the rejection of claims 39 and 58-94 in view of the foregoing arguments and to withdraw the rejection.

Rejection Pursuant to 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 39 and 58-94 stand rejected pursuant to 35 U.S.C. § 112, first paragraph. In the Examiner's view, the specification does not adequately teach a skilled artisan how to practice the invention throughout its full scope.

The Applicants respectfully believe that the Examiner misunderstands what is claimed, particularly in light of the claim amendments made herein. In the following comments, the Applicants first discuss the meaning of the claims as it relates to enablement, and thereafter discuss each of the *Wands* factors analyzed by the Examiner in the Office Action.

The Meaning of the Claims

The Examiner contends that the specification does not adequately teach the genes and polymorphisms that are included within the scope of the claims, and that undue experimentation would be necessary to identify those genes and polymorphisms.

The Applicants believe that one reason the Examiner has made this rejection is that he believes that some of the language which originally appeared in claim 39 can be read very broadly. For example, the Examiner refers to language originally included in item d) of claim 39 in the Office Action at the bottom of page 7. Items d) and e) have been deleted from claim 39. As a result, the enablement provided by the specification for claim 39 must be analyzed with regard to only remaining items a)-c) of claim 39. The Applicants respectfully contend that any concerns the Examiner may have had regarding the breadth of the claims relating to item d) of claim 39 were rendered moot by deletion of that language from the claims. The Examiner is requested to re-evaluate enablement in view of the amended claims. With regard to the amended claims, the Applicants have the following comments.

The Examiner's comments in the Office Action suggest that he believes that practice of the invention would require extensive research to discover previously unknown DAPs. The Applicants believe that the Examiner's comments stem from a misunderstanding of what the Applicants have invented and a misunderstanding of one of the terms used in the claims.

The Applicants' invention is not simply a collection of previously unknown polymorphisms. In fact, all of the polymorphisms disclosed in the specification were previously known by others. Furthermore, occurrence of each of those polymorphisms was correlated by others with a disease or some other pathological condition in humans. Hundreds of thousands of polymorphisms are known to occur in humans (and more are constantly being discovered). What the Applicants have created is an appreciation of the sub-class of polymorphisms that are relevant for predicting the susceptibility of an individual to OS. The relevant polymorphisms are those which i) occur in genes of the classes listed in items a-c of claim 39 and ii) are associated with a disease or pathological state (i.e., ANY disease or pathological state).

The Applicants have identified at least 18 genes (i.e., items i-xvii in claim 62) that are in one or more of the classes listed in items a-c of claim 39. The Applicants do not know whether additional human genes that are in one or more of the classes listed in items a-c of claim 39 will be discovered. It would, however, be immediately apparent to a skilled artisan whether such a newly-discovered gene is in one of those classes once the gene was identified.

Similarly, the Applicants have identified (on pages 12 and 13 of the specification) at least 16 DAPs that have been identified in the genes described in the preceding paragraph. The Applicants do not know whether any additional polymorphisms in those genes will be discovered to be correlated with a disease or pathological state (i.e., whether additional DAPs will be discovered in those genes). However, as soon as such a correlation were made, it would be immediately apparent to a skilled artisan that the polymorphism is a "disorder-associated polymorphism."

In short, the Applicants have discovered the characteristics of polymorphisms that are informative with regard to the susceptibility of an individual human to OS. They have identified the polymorphisms known to them that meet those characteristics. They have not necessarily identified every possible DAP in the relevant genes, and have thus not explicitly taught every conceivable embodiment of their invention. However, they are not required to do so. Patent applicants are not required to disclose every conceivable starting material which can be used in a claimed method - particularly where the claimed method is one of general applicability to starting materials which might be developed or discovered after filing of the application.

At the time a skilled artisan wishes to analyze occurrence of a polymorphism in a human's genome, the polymorphism

A) will occur in a gene in one of classes a-c of claim 39 OR

B) will not occur in such a gene

AND

I) will have been correlated with occurrence of a disease or pathological state (e.g., using the NCBI's SNP database) OR

II) will not have been so correlated.

Thus, a skilled artisan will easily be able to tell whether both A and I are true. If so, then the polymorphism is a "disorder-associated polymorphism" as recited in claim 39. Analyses of which of A and B is true and which of I and II is true are well within the level of skill in the art. Thus, the Applicants are not required to explicitly list this information for each of the hundreds of thousands of known human polymorphisms or to list all known or hereafter-discovered polymorphisms for which both A and I are true.

The Examiner's citation of the *Genentech Inc. v. Novo Nordisk* case (42 USPQ2d 1001) is relevant in this regard. In the *Genentech* case, the patentee had proposed a method of producing a protein (i.e., by expressing a fusion protein and thereafter cleaving the non-desired portion from the protein), but did not disclose any method of actually performing the method. Instead, the patentee simply contended that the necessary technology was known in the art. The court held that, "*While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.*" (*Genentech* at 1005). The patentee described neither appropriate starting materials nor any particular procedure for performing the claimed methods.

In contrast, the Applicants in the present application have described no fewer than 16 particular DAPs (i.e., appropriate starting materials) that can be analyzed to assess an individual's susceptibility to OS. Furthermore, identification of additional DAPs (i.e., identification of additional appropriate starting materials) in the genes recited in the claims is straightforward. By way of example, the Applicants have included the relevant portions of records obtained from the Online Mendelian Inheritance in Man database for two of the genes explicitly recited in the claims (SOD1 and TNF). DAPs are disclosed in those records as well as in records obtainable from such other sources as The SNP Consortium and the National Center for Biotechnology Information. Analytic methods for detecting any desired genetic sequence (i.e., particular procedures for performing) in a human are well known and require no experimentation once the desired sequence is selected. Furthermore, several such procedures are described in the specification (e.g., in paragraphs **[0049]** to **[0055]** on pages 17 to 19 of the specification). For these reasons, the Applicants respectfully contend that the specification

teaches a skilled artisan both appropriate starting materials and particular methods for assessing a human's susceptibility to OS.

The Applicants believe that the Examiner's concerns regarding enablement stem in part from a misunderstanding of the meaning of "disorder-associated polymorphism." This term is defined in paragraph **[0019]**, on page 7, lines 15-17 of the specification. Per that definition, DAPs include only those polymorphisms for which occurrence of the alternative form has been correlated with a disease or pathological state. For this reason, any concern the Examiner may have relating to whether the claims are sufficiently enabled with regard to DAPs that have not yet been discovered is misplaced. Such polymorphisms are not within the scope of the claims (i.e., because they are not DAPs, as defined) until they are discovered and correlated with a disease or pathological condition, at which time their utility in the claimed methods becomes immediately apparent to a skilled artisan. Thus, the Applicants have enabled skilled artisans to practice the claims throughout their entire scope, even though future research may reveal embodiments of the claimed methods (i.e., new DAPs in relevant genes) that cannot be explicitly described at this time.

Wands Factors

The Examiner's comments in the Office Action included a discussion of the *Wands* factors which did not take into account the clarifications made above and the amendments made to the claims herein. The Applicants review the *Wands* factors below, taking these clarifications and amendments into account.

Breadth of the Claims

The Examiner suggests that the claims can encompass hundreds or thousands of genes. In view of deletion from claim 39 of items d) and e), the Applicants believe that the Examiner's suggestion is not valid. The specification discloses 18 genes known to be within the classes a)-c) recited in claim 39, and indicates the class(es) to which each of the genes corresponds in the specification at paragraphs **[0034]**, **[0036]**, and **[0037]**, for example. As disclosed above, skilled artisans are able to readily identify DAPs that occur in such genes. Thus, the claims encompass only known genes and genes which a skilled artisan would be able

to immediately identify as a member of one of the classes recited in the claims upon identification of the gene. The claims encompass only polymorphisms for which a correlation with a disease or pathological state has been established or can be established using information readily available (e.g., in publicly-accessible databases) to skilled artisans (i.e., DAPs). For these reasons, the Applicants respectfully contend that the breadth of the claims is commensurate with what is explicitly disclosed in the specification, as can be readily supplemented by knowledge of those skilled in the art.

Nature of the Invention

Assessment of whether an individual's genome comprises a particular polymorphism is straightforward and can be performed by any of several known methods. The Examiner does not appear to dispute this fact. The Examiner's enablement rejection appears to be based on a contention that a skilled artisan would not know which polymorphisms to assess in view of the specification. The Applicants respectfully reply that the specification teaches which polymorphisms should be assessed: two, four, six, ten, fifteen or more DAPs that occur in the genes indicated in the specification. As noted above, the identities of appropriate genes include those explicitly listed in the specification and genes which would immediately be recognized by a skilled artisan as being within one of the classes of genes recited in the claims. Also as noted above, DAPs include only those for which a correlation between occurrence of the polymorphism and a disease or other pathological condition has been made. Thus, the Applicants have adequately taught skilled artisans which polymorphisms to assess, and the knowledge of skilled artisans permits assessment of those polymorphisms.

The Applicants have provided skilled artisans with the critical information regarding which polymorphisms to assess: i.e., DAPs in the genes of the recited classes.

State of the Prior Art

The Examiner cites the Forsberg article (Forsberg et al., 2001, Arch. Biochem. Biophys. 389(1):84-93) for the proposition that correlating occurrence of a polymorphism with a phenotypic consequence is difficult and unpredictable.

The Applicants reply that Forsberg represents precisely the type of thinking that the present invention has overturned. By analogy, Forsberg concentrates so intently on individual trees (phenotypic effects attributable to individual polymorphisms) that the forest (overall susceptibility to OS) is not perceived. Forsberg is not the only prior art that suffers from this myopia.

The Applicants have made the important discovery that it is not necessary to thoroughly understand the causative link between occurrence of a polymorphism and the corresponding incremental change in susceptibility to OS. Instead (continuing the analogy), it is sufficient to observe the density of the forest (i.e., occurrence of DAPs in appropriate genes) rather than studying individual trees and how they might interact with one another.

Put another way, the Applicants have discovered that at least one solution to the problem of assessing an individual's susceptibility to OS is far simpler than previously believed. Instead of trying to understand the interplay between many genes involved in the body's response to OS and how various individual polymorphic forms of those genes might interact with one another (i.e., understanding which will likely never be fully achieved by the scientific community, at least in the near future, for so complex a system as the body's response to oxidative stress), the Applicants have discovered that a suitable estimate (for the purpose of formulating anti-oxidant compositions) of an individual's susceptibility to OS can be made simply by assessing several relevant genes. If the individual's genome includes a form of one or more of these genes that are sufficiently 'bad' that a disorder is correlated with that form, then that indicates that the function of that gene is impaired (wholly or partially) and that the individual is more susceptible to OS than an individual whose genome does not include the disorder-associated form of the gene.

The present invention demonstrates that much of the prior art was too caught up in the details of how a genetic change exerts phenotypic effects to be able to predict those phenotypic effects in a simple, readily-assessable way. The prior art simply did not appreciate that the Applicants' elegantly simple methods have the claimed use, as indicated by the Examiner's failure to find anticipatory or obviating references.

The Level of Skill in the Art

The Examiner recognizes that the level of skill in this art is relatively high. The simplicity of the claimed methods (i.e., assessing occurrence of polymorphisms in an individual's genome) places the invention firmly within the level of skill in the art.

The Amount of Direction Provided by the Inventors

The Applicants have provided at least 28 examples of suitable genes (see claim 62) for which assessing occurrence of DAPs is appropriate for assessing susceptibility to OS. The Applicants have explicitly listed most or all of the known genes that are within the classes a)-c) recited in claim 39. The Applicants have also listed no fewer than 18 DAPs that are appropriate for assessing susceptibility to OS (see pages 12 and 13 of the specification). Skilled artisans can readily find additional DAPs, as exemplified in the enclosed OMIM database records (which were obtained simply by searching for gene names "SOD1" and "TNF"). The Applicants respectfully contend that they have provided sufficient disclosure that skilled artisans are able to practice the invention for any known or hereafter-discovered gene in the classes a)-c) recited in claim 39 and for any DAP in those genes.

The Existence of Working Examples

The Examiner correctly observes that the specification does not include working examples. For reasons discussed in this Amendment, the Applicants respectfully contend that skilled artisans can practice the claimed methods without studying working examples.

The Quantity of Experimentation Needed to Make or Use the Invention

The Examiner contends in the Office Action that substantial experimentation is needed to perform the claimed methods. The Applicants strenuously disagree.

The specification lists the genes known to be within the classes a)-c) recited in claim 39. DAPs (as defined in paragraph **[0019]** on page 7, lines 15-17) in those genes are either explicitly listed in the specification or readily available to skilled artisans by searching publicly-available databases. Methods of assessing whether a selected polymorphism occurs in a human's genome are routine. Appropriate amounts of anti-oxidants for administration to

normal humans (i.e., humans who do not exhibit unusual susceptibility to OS) are known, and it would be immediately apparent to a skilled artisan to increase the amount of the anti-oxidant in individuals found to have heightened susceptibility to OS.

The Examiner's comments relating to 'unpredictability' and the 'need for experimentation' appear to stem from the Examiner's recognition that future research may reveal the existence of additional genes that fall within classes a)-c) recited in claim 39 (e.g., a second human paraoxonase gene) or additional DAPs in such genes. The Applicants respectfully contend that this concern is misdirected, since assessment of DAPs cannot (per the definition in paragraph **[0019]** on page 7, lines 15-17) fall within the scope of the claims unless and until a correlation between occurrence of the polymorphism and a disease or other pathological condition is established. At that point, it would be immediately obvious to a skilled artisan (i.e., without any experimentation) that the DAP is one that can be used in the claimed methods.

For the foregoing reasons, the Applicants respectfully contend that substantially no experimentation is necessary to practice the claimed methods throughout the full scope of what is claimed.

For the foregoing reasons, the Applicants respectfully contend that when the claims are read in view of the meanings given the claim terms by the Applicants, there can be no doubt that skilled artisans are able to practice the claimed methods substantially without any experimentation. The specification adequately enables the claims for that reason. Reconsideration and withdrawal of the Examiner's rejection of claims 39 and 58-94 pursuant to 35 U.S.C. § 112, first paragraph (enablement) are respectfully requested.

Summary

For the reasons set forth above, the Applicants respectfully contend that each of claims 39, 60-85, and 87-97 is in condition for allowance. Reconsideration and withdrawal of each of the Examiner's rejections are requested. If the Examiner concurs, he is requested to telephone the Applicants' undersigned representative to request authorization to cancel withdrawn claims 1 and 40 prior to issuance of a Notice of Allowance.

Respectfully submitted,

John R. DePhillipo et al.

27 May 2003
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By: _____

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Enclosures: Petition for a Three-Month Extension of Time
OMIM Search Results for "SOD1"
OMIM Search Results for "TNF"